Summary Minutes of the
Antiviral Drugs Advisory Committee
Hilton Hotel, Silver Spring, Maryland
8727 Colesville Road, Silver Spring, Maryland.
June 2, 2010

All external requests for the meeting transcripts should be submitted to the CDER, Freedom of Information office.

These summary minutes for the June 2, 2010 Meeting of the Antiviral Drugs Advisory Committee of the Food and Drug Administration were approved on Jan. 27, 2011

I certify that I attended the June 2, 2010 meeting of the Antiviral Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
Paul T. Tran, RPh.	Craig Hendrix, M.D.
Designated Federal Official, AVDAC	Committee Acting Chair

The Antiviral Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on June 2, 2010 at the Hilton Hotel, Washington DC/Silver Spring, 8727 Colesville Road, Silver Spring, Maryland. Prior to the meeting, the members and the invited consultants had been provided the background material from the FDA. The meeting was called to order by Craig Hendrix, M.D. (Acting Chair); the conflict of interest statement was read into the record by Paul Tran, R.Ph. (Designated Federal Official). There were approximately 150 persons in attendance. There was no speaker for the Open Public Hearing session.

Attendance:

Antiviral Drugs Advisory Committee Members Present (Voting):
Craig Hendrix, M.D., Amneris Luque, M.D., Victoria Cargill, M.D., M.S.C.E., Patrick Clay, Pharm.D.

Endocrinologic and Metabolic Drugs Advisory Committee Members Present (Non-voting):
Enrico Veltri, M.D. (Industry Representative)

Special Government Employee Consultants Present (Voting):
Athena Zuppa, M.D., M.S.C.E., Curt Hagedorn, M.D., Michelle Roland, M.D., Shawn Ralston, M.D., Doris Strader, M.D., Susan Ellenberg, Ph.D., Prescott Atkinson, M.D., Yoshihiko Murata, M.D., Ph.D., Angelica Walden, MBA (Patient Representative), Peter Havens, M.D., Yvonne Maldonado, M.D.

Regular Government Employee Consultants Present (Voting):
Alexandra Freeman, M.D., Barney Graham, M.D., Ph.D.

FDA Participants:
Edward Cox, M.D., M.P.H., Debra Birnkrant, M.D., William Tauber, M.D., Alan Shapiro, M.D., Ph.D., Jules O'Rear, Ph.D.

Open Public Hearing Speakers:
None

Designated Federal Official:
Paul Tran, R.Ph.

Issue: The committee discussed a Biologics License Application (BLA 125283), motavizumab, single-dose liquid solution 50 mg/0.5 mL and 100 mg/1 mL vials, MedImmune, for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in children at high risk of RSV disease.

Call to Order Introduction of Committee	**Craig W. Hendrix, M.D.** Acting Chair AVDAC
Conflict of Interest Statement	**Paul T. Tran, R.Ph.** Designated Federal Official, AVDAC
FDA Opening Remarks	**Debra B. Birnkrant, M.D.** Director Division of Antiviral Drug Products (DAVP) Office of New Drugs (OND), CDER, FDA
Applicant Presentation	**MedImmune, LLC**
Regulatory Affairs, Introduction	**Ross Lobell** MedImmune
RSV Overview	**Octavio Ramilo, M.D.** Nationwide Children's Hospital
Clinical Development, Efficacy	**Pamela Griffin, M.D.** MedImmune
Clinical Development, Safety	**Genevieve Losonsky, M.D.** MedImmune
Risk Assessment	**Mark Boguniewicz, M.D.** Immunology Professor National Jewish Health University of Colorado Denver School of Medicine
Benefit Assessment	**Octavio Ramilo, M.D.** Nationwide Children's Hospital
Clinical Development, Post Approval Commitments	**Gregory Geba, M.D., M.P.H.** MedImmune
Clarifying Questions to Applicant	
Break	
FDA Presentation	**Alan Shapiro, M.D., Ph.D.** Medical Officer DAVP, OND, CDER, FDA
Clarifying Questions for FDA and Applicant	

Lunch

Open Public Hearing Session

Charge to the Committee **Debra B. Birnkrant, M.D.**

Questions for Discussions

Adjournment

Questions to the Advisory Committee:

1) Please comment on the safety profile of motavizumab, specifically with respect to the potential for hypersensitivity reactions including life-threatening anaphylaxis.

There was a clear signal of skin/hypersensitivity reactions with motavizumab. There was a suggestion of an immunological basis for these hypersensitivity reactions which will need to be further studied. Some committee members felt that, with appropriate warnings in labeling, hypersensitivity reactions could be managed without resultant severe toxicities. Since no patients were hospitalized or died due to hypersensitivity reactions in motavizumab's clinical studies, it was not clear what the frequency of severe anaphylactic reactions would be if motavizumab was used in a larger number of patients. There was a lack of "sicker patients" enrolled into these studies as compared to the earlier trial of palivizumab. There was a concern that in a sicker population, there might be more frequent and more severe hypersensitivity reactions. There was a general consensus that more information is needed, the key issue being whether the information should be gathered pre or post-marketing.

Several panel members indicated that it would be useful to have an additional option for the prophylaxis of RSV if this product was approved and available on the market. In contrast, others were concerned that there would not be options if the sponsor planned to withdraw palivizumab with the approval of motavizumab.

Please see transcripts for detailed discussion.

2) Do the data from the applicant's studies adequately support the efficacy of motavizumab for the prevention of serious lower respiratory tract infection with RSV in at risk infants?

There was a general consensus that motavizumab prevents RSV hospitalizations. Several members felt that Motavizumab was not better than the other available treatment option of Palivizumab, but most felt that it's as effective as Palivizumab. Many panel members questioned the rationale for the non-inferiority design of the supporting studies. These panel members wondered why the trials were not designed and powered to show superiority of motavizumab over palivizumab rather than just showing non-inferiority.

The committee also asked about subset analyses and indicated their useful role to identify a "sicker" niche of the pediatric population who may have a more favorable risk-benefit ratio for motavizumab. Motavizumab could then be indicated for the identified subset of patients in labeling. There was also interest by some committee members in post-marketing studies to help identify the subset of patients with the favorable risk-benefit ratio. Other committee members suggested the benefits of a larger pre-marketing study to answer some of these questions to sort out indication niches and superiority issues.

Please see transcripts for detailed discussion.

3) Given the potential benefits and risks, should motavizumab be licensed for marketing?

Vote: Yes: **3** No: **14** Abstain: **0**

Please discuss the rationale for your vote.

1. If no, what additional data/studies can be provided to support the licensing of motavizumab?

2. If yes, are there post-marketing studies needed to provide data that would a) provide additional safety data or b) optimize use of motavizumab?

There were a lot of difficulties in making the licensure decision for this product. There was a general consensus that there are many questions still to be answered in additional clinical studies. Some members were concerned they did not have enough information to explain the risks and benefits of motavizumab versus palivizumab to patient families and would feel uncomfortable recommending motavizumab. Whether additional studies should be done pre or post-marketing was an important issue that affected the votes for many members of the committee. The recommendations for pre-marketing studies are similar to the recommendations for post-marketing studies, that is, more details are needed to sort out which populations are most likely to benefit from use of the drug to guide appropriate labeling and so better understand the risk, severity, and management of the hypersensitivity reactions to mitigate risk to patients. Pre-marketing studies were favored by those members who voted no and these members also recommended looking at sicker and larger patient populations to define the role of the product, namely, to identify the patients most likely to benefit from using motavizumab since the existing option (palivizumab) clearly has less toxicity. The additional larger studies would also better define the hypersensitivity risk frequency and severity and evaluate the possibility for progression to more serious toxicity.

Please see transcripts for detailed discussion.